

# Autoregulation of a Total Artificial Heart in Man

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## Introduction

From May of 1981 to December 1982 five human subjects declared brain dead by established medical criteria were taken to the operating room. Their hearts were replaced with the Utah Total Artificial Heart (U-TAH)<sup>a</sup> and allowed to function for 1½ to 72 hours. While in no way resembling human tissue, each pneumatic ventricle behaves according to a physiological principle, the Starling mechanism. The principle relating diastolic volume to the work of ventricular ejection has been abstracted and applied in this study to the autoregulatory function of the two pneumatic ventricles in the human circulatory system (See Figures 1 & 2). Although self regulatory capabilities have been

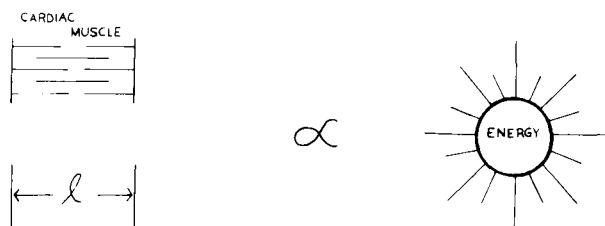


FIGURE 1. An increase in filling pressure will lengthen the myocardial fiber. The result is an increase in contractility and increased stroke volume of the natural heart.

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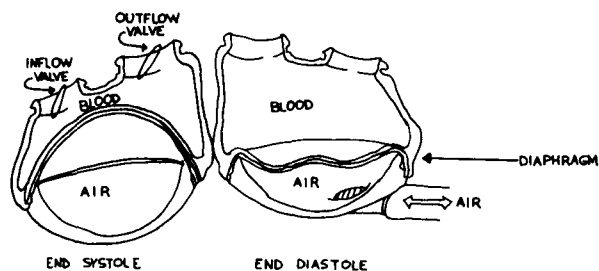


FIGURE 2. Increase in venous pressure displaces the flexible diaphragm towards its maximal diastolic position resulting in increased stroke volumes of the artificial heart. The maximum systolic position is shown in the far left half of the drawing.

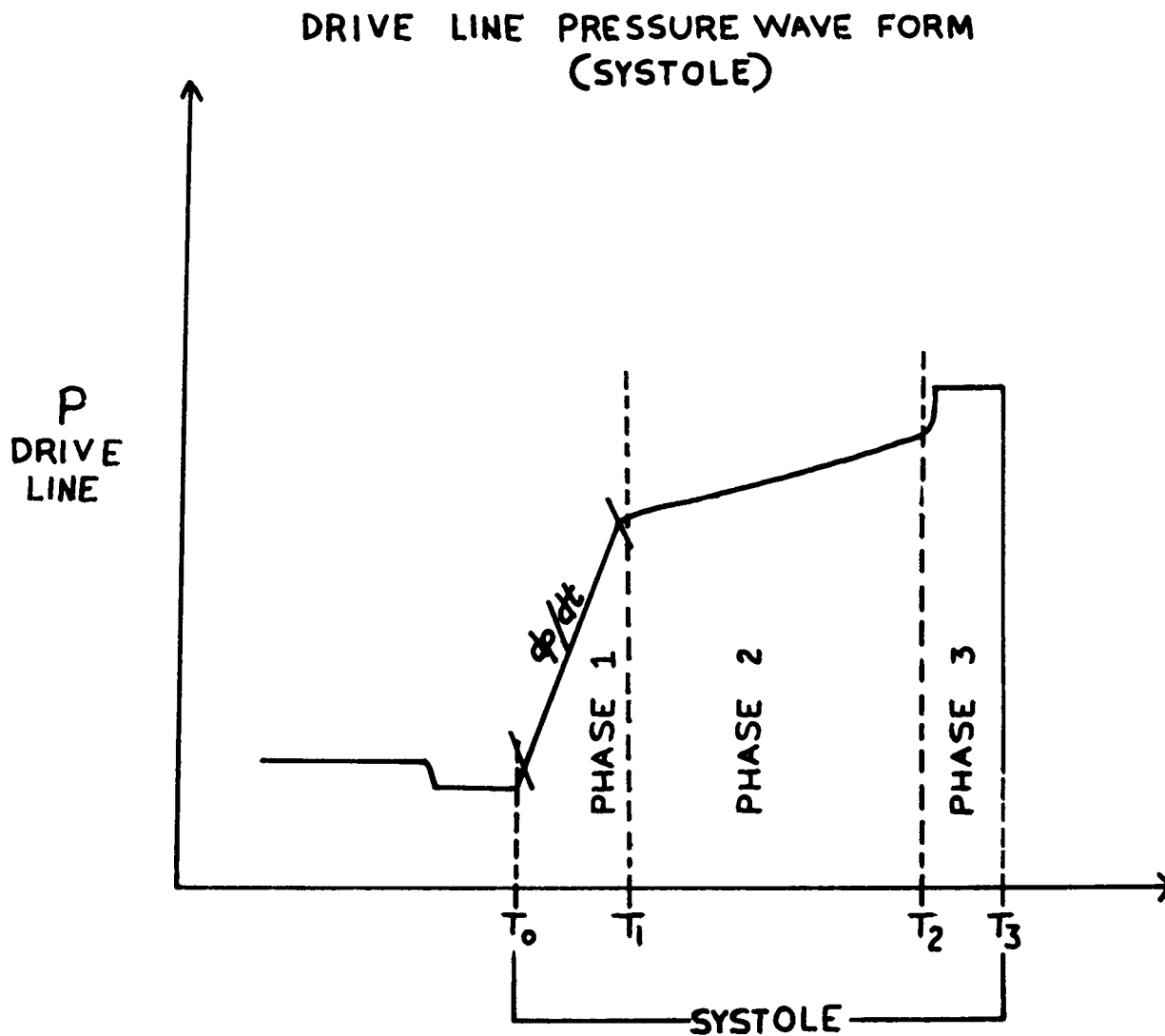
documented in the laboratory and are also evident in animal studies, this study documents these capabilities in man.<sup>1,2</sup>

## Methods

Subjects were placed on cardiopulmonary bypass and implanted with the U-TAH ventricles under sterile conditions for anatomic and functional studies. In three of the subjects, the sternum was closed and they were subsequently transferred to the surgical intensive care unit (SICU). As during cardiopulmonary bypass, adequacy of perfusion was accessed by measuring arterial and venous blood gases and urine output. Throughout the post-operative period, right and left atrial and radial artery pressures were continuously monitored. Studies on cardiac output were then conducted in the SICU.

Provided with a source of compressed air and vacuum the Utah Heart Drive (UHD) regulates pressure and vacuum pulses to each ventricle. While heart rate and percent systolic time are the same for both, the driving pressure and vacuum to each ventricle is set independently. Ventricular function is monitored on the air side of the diaphragm.

The pressurized or systolic phase is represented by left and right air pressure wave forms derived from transducers on the air output line from the UHD. In Figure 3 the time from T<sub>0</sub> to T<sub>3</sub> is systole,



**FIGURE 3.** Air Pressure vs Time profile of the air in the drive line connecting the ventricle with the heart driver. The systolic portion of the cardiac cycle is divided into three phases. The first is isovolemic pressurization to arterial pressure. The outflow valve opens at  $T_1$ . Ejection occurs in Phase II until the diaphragm is in maximum systolic position. Phase III indicates air pressure in the air compartment of the ventricle after completion of the stroke volume and its pressure indicates that the maximum systolic diaphragm position has been achieved.

the length of which depends on the heart rate and percent systole set on the UHD. During Phase I pressure rises to a level sufficient to open the outflow valve against arterial pressure. From  $T_1$  to  $T_2$ , Phase II, blood is ejected from the ventricle. At  $T_2$  the blood from the previous diastole has been fully ejected. Phase III displays the pressure applied to the diaphragm in excess of the pressure achieved in Phase II. Phase III aids optimization of the percent systolic time. Once this phase is

reached there is no reason to prolong it. The more time allotted for systole, the less time available for diastolic filling.

The diastolic phase is monitored on the exhaust port of the UHD by two Fleisch pneumotachometers.<sup>b</sup> The outputs are displayed on an Apple<sup>c</sup> Computer Terminal which derives stroke volumes and cardiac outputs for each ventricle.<sup>3</sup> In Figure 4 the curve displays the flow of air out of the air chamber of the ventricle. The air is being displaced, volume per volume, by blood in the blood chamber. Diastolic time ( $T_0 - T_3$ ) is a function of rate and percent systole set on the UHD. By numer-

<sup>b</sup>OEM Medical, 8741 Landmark Road, Richmond, VA 23261

<sup>c</sup>Apple Computer, Inc., 10260 Bandle Drive, Cupertino, CA 95014

## DRIVE LINE AIR FLOW WAVE FORM

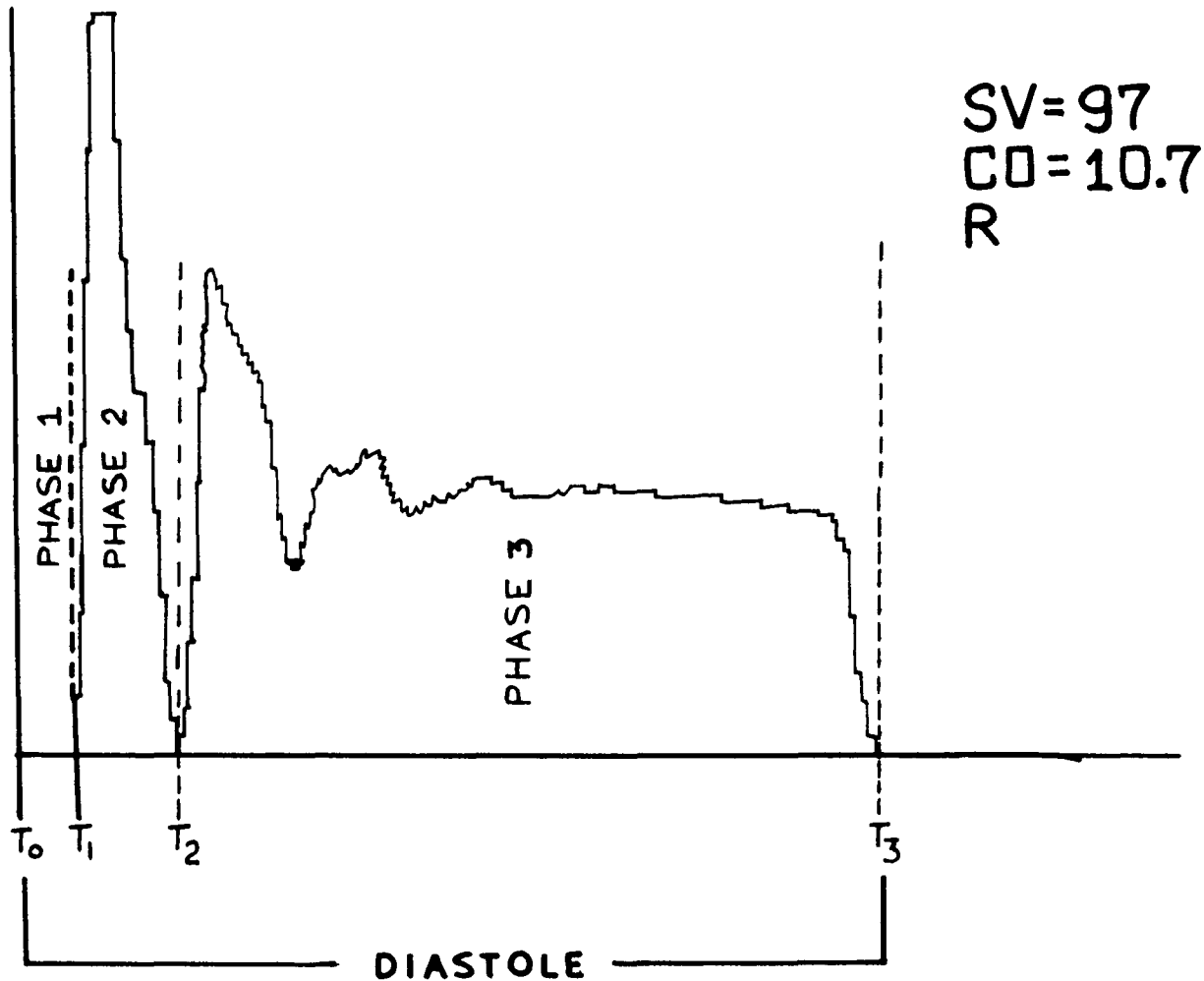


FIGURE 4. Air flow vs. Time profile of the air exhausting from the driveline connecting the ventricle with the heart driver. The diastolic portion of the cardiac cycle is divided into three phases. The first is attributed to mechanical delay. At  $T_1$ , the beginning of Phase II, the exhaust valve in the Utah Heart Driver opens and allows the pressurized air chamber to equilibrate with the atmosphere. Diastolic filling occurs in Phase III until the time allotted for diastole is completed or the ventricle is completely filled, whichever occurs first.

ically integrating the curve from  $T_2$  to  $T_3$ , the actual blood filling time, the Apple Computer derives stroke volume and calculates cardiac output.  $T_0 - T_1$  is a mechanical delay of the system.  $T_1$  to  $T_2$  displays the escape of pressurized air from the previous systole. Filling of the heart cannot occur until the pressure returns to atmospheric level at  $T_2$ . (The air escaping during Phase II of diastole is the air pressurized during Phase III of systole). It should be noted that a full ventricle at the end of diastole is not conducive to autoregulation.

To obtain function curves of the left ventricle under various values of heart rate, vacuum, and PEEP, left atrial pressure was varied from zero to maximum by varying the right ventricular driving pressures between 0 and 100 mmHg. We were thus able to observe left ventricular response to differing venous returns from the right ventricle. With the left sided driving pressure and percent systole held constant, Frank-Starling curves were constructed for different heart rates, vacuums and PEEP values by plotting left ventricular output vs. left atrial

pressure.

## Results

The results are best presented as function curves. The effect of rate, vacuum and PEEP are illustrated in the following figures. The change of the function curves caused by a change in rate is shown in Figure 5. Increases in rate primarily affect the maximum cardiac output achievable. A heart rate

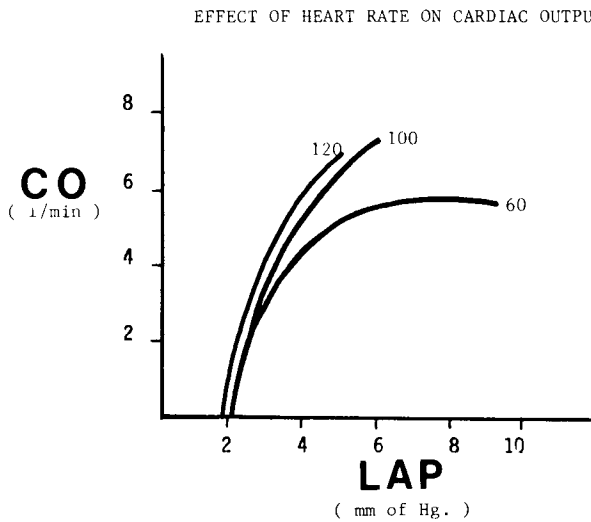


FIGURE 5. Increasing the rate increases the maximum achievable ventricular output. It is apparent from the curve that once a plateau has been reached for a given rate, in order to increase output, one must increase the rate.

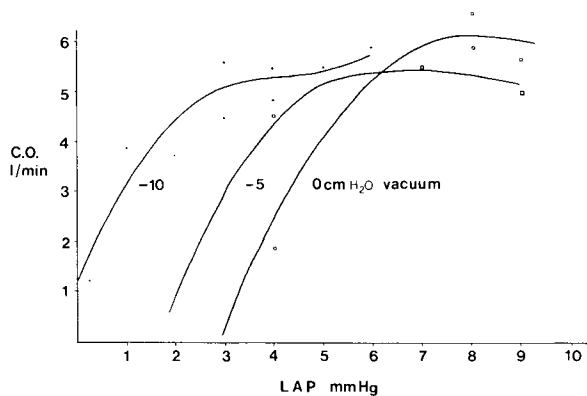


FIGURE 6. An increase in vacuum applied during diastole produces a shift of the curve to the left, allowing equal cardiac outputs at lower atrial filling pressures.

of 60 could yield a maximum output of 6.0 liters/minute whereas a heart rate of 120 could increase this to a theoretical value of 12.0 liters/minute. In reality we only pumped to 7.5 liters/minute because of limitations of right ventricular flow.

The effects of vacuum applied to the air side of the diaphragm during diastole are illustrated in Figure 6. Increasing vacuum shifts the function curve to the left. The new function curve allows the same cardiac output to occur with lower left atrial pressure.

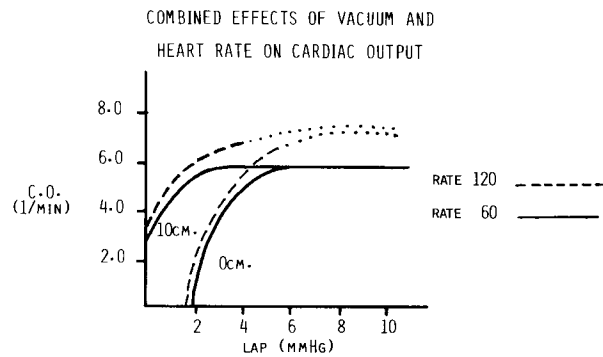


FIGURE 7. Combining the effects of vacuum and increased rate demonstrates that vacuum shifts the curve horizontally and rate shifts the function curves vertically.

The combined effects of vacuum and increased heart rate are illustrated in Figure 7. Increasing heart rate shifts the curve in a manner reminiscent of the effect seen with increased sympathetic stimulation.<sup>4</sup> Vacuum moves the curve to the left. Combining the curves demonstrates that vacuum shifts the curve horizontally and rate shifts the function curves vertically.

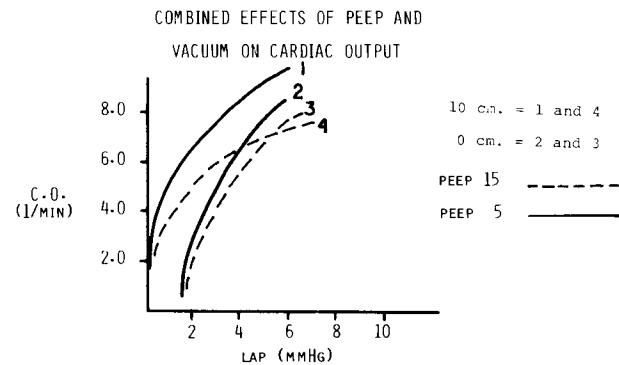


FIGURE 8. PEEP lowers cardiac output. Combining PEEP and high vacuum can markedly decrease cardiac output.

Figure 8 illustrates the effects of PEEP and vacuum on cardiac output. For a given filling pressure, PEEP lowers cardiac output. Combining PEEP with high vacuum has a particularly noticeable effect in lowering cardiac output.

## Discussion

Guyton has used cardiac function curves for

quantifying the natural heart's ability to pump blood. He makes the point that while a multitude of variables interact to determine cardiac output, one can plot function curves relating cardiac output to one variable at a time.<sup>4</sup> Analyzing data from Guyton, Michael Crosby postulated the influence of various factors on cardiac output.<sup>5</sup> He found that while cardiac output is effected by sympathetic and parasympathetic stimulation, venous return and arterial resistance, venous return is the dominant factor in the regulation of cardiac output. Eighty-one percent of the increased cardiac output during moderate exercise is due to the effect of venous return.

When the natural heart increases its rate both right and left ventricles respond similarly; thus, that is not the mechanism by which autoregulation of outputs between the two ventricles is maintained. To use rate to achieve this purpose the ventricles would have to be uncoupled and each would need to be a variable rate pump with a separate device. Such a solution was tested in Dr. Nosé's laboratory at the Cleveland Clinic.<sup>8</sup> He found that the system provided optimal regulation of right and left cardiac output. The price was the electrical support system needed for control.

In developing an artificial heart at the University of Utah, Dr. Clifford Kwann-Gett designed a ventricle incorporating a pneumatically driven diaphragm as a pumping element.<sup>1</sup> His objective was to satisfy two requirements, the generation of physiological cardiac output curves and the avoidance of cumbersome electrical control and feedback mechanisms; that is, a heart with inherent autoregulation.<sup>7</sup> Upon implantation in sheep he found that the pneumatic ventricle responded to increases in atrial filling pressure with increased output. The ventricle achieved blood pressure stability and regulation of blood flow without electrical feedback systems. In 1972, Kwann-Gett's design was modified in several steps by Dr. Robert Jarvik into the present J-7 model designed to fit in the human chest and put into Dr. Barney Clark in December, 1982.

Fortunately, there are a number of heart driving parameters that allow the operator to pick a function curve appropriate for the patient's physiologic requirements. For example, should the patient require a cardiac output greater than 6 liters/minute this could not be achieved on the function curve

shown in Figure 5 for a heart of 60 beats/minute. The operator would have to increase the heart rate to 100 or 120 beats/minute. For each ventricle to remain functioning on the steep portion of the Starling curve, a reserve of air needs to be left in the air chamber of the ventricle at end diastole. Increasing the heart rate from 60 to 120 beats per minute while pumping 6 liters per minutes re-establishes some diastolic reserve. This reserve assures autoregulatory function.

Another physiologic requirement may be the maintenance of as low a left atrial pressure as possible to prevent congestion of poorly functioning lungs. The operator of the TAH can achieve this by increasing the vacuum on the left ventricle thereby maintaining the same left ventricular output at a lower left atrial pressure (See Figure 6). This was required in several of our subjects implanted with the TAH. Occasionally patients require PEEP to augment arterial oxygenation. The effect of PEEP on the natural cardiovascular system has also been demonstrated in our subjects with the TAH. The addition of PEEP depresses the function curve of the ventricle as shown in Figure 7. Awareness of this by the operator of the UHD would allow him to compensate for this depression by several modes of action such as increasing the heart rate or augmenting the vacuum.

In conclusion the understanding of the methods of moving from one function curve to another allows the operator to select one that will maintain self regulatory function of the ventricles with minimal adjustments in the post-operative period.

## References

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